Changes in secondary pharmacological prevention of acute coronary syndromes and stroke after hospital discharge: a 6-month follow-up study of German primary care patients

Loeffert, Sabine; Ommen, Oliver; Ernstmann, Nicole; Pfaff, Holger

Empfohlene Zitierung / Suggested Citation:
Loeffert, S., Ommen, O., Ernstmann, N., & Pfaff, H. (2008). Changes in secondary pharmacological prevention of acute coronary syndromes and stroke after hospital discharge: a 6-month follow-up study of German primary care patients. *Journal of Public Health*, *17*(1), 3-7. https://doi.org/10.1007/s10389-008-0210-0

J Public Health (2009) 17:3–7
DOI 10.1007/s10389-008-0210-0

ORIGINAL ARTICLE

Changes in secondary pharmacological prevention of acute coronary syndromes and stroke after hospital discharge: a 6-month follow-up study of German primary care patients

Sabine Loeffert · Oliver Ommen · Nicole Ernstmann · Holger Pfaff

Received: 31 January 2008 / Accepted: 20 May 2008 / Published online: 17 July 2008

Abstract
Aim This study examined modifications in secondary preventive medication between the time of hospital discharge (HD) and during a 6-month follow-up treatment of outpatients with acute coronary syndromes (ACS) and stroke.
Subjects and methods During a 6-month period, a health diary was completed on a weekly basis by 98 patients who were initially hospitalised with ACS and 29 patients with strokes in the Cologne area (Germany). Changes in medication between the time of HD and follow-up treatment (weeks 2, 12, and 24) were recorded.
Results On average, patients with ACS took six medications, whereas patients with stroke took five medications per day. ACS patients received beta-blockers (96%), lipid-lowering agents (80%), and angiotensin-converting enzyme (ACE) inhibitors (64%) at HD, and no changes in medication were made during follow-up treatment. However, there was a significant decrease in prescriptions of clopidogrel among ACS patients within 6 months, and about 13% of ACS patients did not receive an antiplatelet agent at any time. Stroke patients received beta-blockers (50%), lipid-lowering agents (67%), and antiplatelet agents, such as acetylsalicylic acid (57%) or clopidogrel (27%), at the time of HD, and no significant changes in medication were instituted during follow-up treatment.
Conclusion Treatment of ACS patients with the combination of acetylsalicylic acid and clopidogrel was insufficient, although it has been shown that this combination is highly effective in secondary prevention of ACS. Besides medical reasons, the cost-containment restrictions ("medication budget") for German physicians might explain the observed failure of guideline-oriented medication. Furthermore, no changes in medications occurred regarding blood-pressure- and lipid-lowering agents.

Keywords Acute coronary syndrome · Stroke · Secondary prevention · Primary care

Abbreviations

ACE	angiotensin converting enzyme
ACS	acute coronary syndromes
ATC	Anatomical Therapeutic Chemical (classification system)
HD	hospital discharge
OTC	over the counter (drugs)

Introduction

Changes in medications between ambulatory and stationary treatment have been examined in several publications with regard to interface problems. As a result, modifications in pharmaceutical treatment were found to various degrees and at different stages in the course of continued medical care (Hach et al. 2005; Himmel et al. 2004; Taxis and Schneeweiss 2003). Inconsistency in prescription behaviour is especially problematic when dealing with medications

S. Loeffert · O. Ommen (✉) · N. Ernstmann · H. Pfaff
Center for Health Services Research Cologne,
University of Cologne,
Eupener Str. 129,
50933 Cologne, Germany
e-mail: oliver.ommen@uk-koeln.de

H. Pfaff
Department of Medical Sociology, University of Cologne,
Eupener Str. 129,
50933 Cologne, Germany

with a proven benefit for preventing serious adverse health conditions. For example, the need for pharmaceutical approaches to secondary prevention of acute coronary syndromes (ACS) and stroke have increasingly gained recognition and acceptance during the last 2 decades (Jamieson 2007; Phillips 1999). In this regard, national and international therapeutic guidelines for the prevention of secondary stroke and coronary events have been developed (e.g., Bundesärztekammer et al. 2006; Bertrand et al. 2002; Braunwald et al. 2002; Joint Guidelines issued by the German Neurological Society and the German Stroke Society 2005). As outlined in these therapeutic guidelines, antiplatelet, antihypertensive, and lipid-lowering therapies are known to significantly reduce the risk of recurrence of macrovascular diseases, such as coronary and cerebrovascular diseases. Contrary to this, national and international studies have shown that these guidelines are not yet fully implemented in primary and secondary prevention with respect to platelet aggregation inhibitors, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and statins (EUROASPIRE I and II Group 2001; Krumholz et al. 1998; Welterman et al. 1997) in the prevention of ACS. However, long-term secondary stroke prevention in Germany has revealed better findings, especially with regard to antithrombotic medications (Hamann et al. 2003). Even though therapeutic guideline implementation has improved over the past years (Mandelzweig et al. 2006; Wienbergen et al. 2001), only few studies in Germany have examined whether treatment recommendations after hospital discharge were according to current guidelines and to what extent these recommendations were realised in subsequent primary care (Zeymer et al. 2007). The goal of this study was to compare treatment recommendations for secondary pharmacological prevention of ACS and stroke after hospital discharge with current guidelines and to examine changes in medication between initial hospitalisation and continued medical care.

Methods

Patients with ACS or stroke, who were treated in five hospitals in the Cologne area (Germany) between April 2005 and November 2005, were observed for 6 months after hospital discharge in a prospective study. Inclusion criteria for the study were as follows: admission diagnosis of ACS, as coded for by the hospital's administrative database (ICD-10 codes I20.0, I20.8, and I21); admission diagnosis of cerebral infarction or stroke (ICD-10 codes I63 and I64); and age >18 years with the cognitive and intellectual capability to participate in the study. Of the initially 970 hospitalised patients, 408 were excluded due to meeting the exclusion criteria: (1) very poor general health condition (35%), (2) low cognitive capability (14%), (3) lack of substantial knowledge of the German language (15%), (4) participation in other clinical studies (3%), and (5) other reasons (7%), or (6) due to early hospital discharge (26%). Of the remaining 562 potentially qualified patients, 216 (38%) gave their consent to participate in the study. The dropout rate of the included 216 patients totalled 41%. Patients` reasons for drop out were: (1) "no longer interested" (69%), (2) "poor general health condition" (18%), (3) "too time-consuming" (8%), and (4) "too difficult" (6%). Thus, the remaining study population consisted of 127 patients (98 patients with ACS and 29 patients with stroke).

Data acquisition was pursued in three steps. During the initial hospitalisation or shortly after, patients completed a standardised questionnaire (step 1). The questionnaire captures socio-demographic data and information regarding the patient's general health. At the time of hospital discharge, each patient was given a questionnaire with a weekly health diary (step 2). The appropriate questionnaire was filled in by the patients on a weekly basis for 6 months following HD. The questionnaire covered aspects of general health, medications (brand name), dosing, change in medications, and the underlying reasons for medication changes. The third step of data acquisition was conducted by a study nurse for case documentation. Following a standardised procedure, information regarding admission and HD diagnosis (ICD-10), medications, stationary diagnosis and therapy, and follow-up treatments were obtained from the patient's medical records and HD summary.

The medication was classified according to the WHO's Anatomical Therapeutic Chemical (ATC) classification system (Dimdi 2005). Over-the-counter (OTC) drugs, topical medications, acute medications (e.g., antibiotics, immunmodulatories, and antineoplastics), homoeopathic medications, herbal agents, and enzymes were not included in the study. Statistical analyses were performed using SPSS 12.0 and 15.0 (Statistical Package for the Social Sciences). Patient characteristics and medication data are presented in absolute and relative frequencies. In addition, for each medication a Cochran's Q test was performed to test for differences between the frequencies of prescription over time. An α-adjustment (0.05) for multiple testing was performed by means of the Bonferroni procedure (Table 2). Due to the small sample size of this study, all available complete data sets were used for statistical analysis. Therefore, there were 104 ACS patients enclosed at hospital discharge and week 2 and 30 stroke patients from HD until week 12.

Results

The demographic characteristics of the patient groups are presented in Table 1. Patients with ACS took an average six

Table 1 Patient characteristics at hospital discharge

		Acute coronary syndromes	Stroke
Gender	Male	73.1% (76)	60.0% (18)
	Female	26.9% (28)	40.0% (12)
Admission diagnosis	Acute myocardial infarction (I21)	34.6% (36)	
	Unstable angina (I20)	65.4% (68)	
	Cerebral infarction (I63)		80.0% (24)
	Stroke, not specified (I64)		20.0% (6)
Hospital	Tertiary care	85.6% (89)	30.0% (9)
	Primary care	10.6% (11)	63.3% (19)
	Comprehensive care	3.8% (4)	6.7% (2)
Native language	German	92.3% (96)	100.0% (30)
	Other	7.7% (8)	0%
Age	<=40 years	3.8% (4)	0%
	41–50 years	13.5% (14)	10.0% (3)
	51–60 years	23.1% (24)	16.7% (5)
	61–70 years	39.4% (41)	46.7% (14)
	71–80 years	17.3% (18)	23.3% (7)
	>=81 years	2.9% (3)	3.3% (1)
Length of hospitalisation	Median (days)	4	9
	Minimum (days)	1	3
	Maximum (days)	30	34

medications per day within the observation period (minimum at week 24=0 and maximum at week 24=14), whereas patients with a stroke took five different medications per day (minimum at week 24=1 and maximum at week 24=10).

Of all patients with ACS, 100 (96%) received a beta-blocker, 16 (15%) used a vasodilator used for cardiac disease (organic nitrates and other vasodilators, e.g., molsidomine and trapidil), 83 (80%) used a lipid-lowering agent, and 67 (64%) used an ACE inhibitor at the time of HD. Eighty-nine (86%) of all study patients with ACS used acetylsalicylic acid and 58 (56%) clopidogrel as antiplatelet agents at the time of HD (Table 2). No change in medications was observed 2 weeks following HD. In week 24, a minor increase in the use of vasodilators 18% ($p=0.188$) and a slight, however, due to the adjusted α-level ($\alpha^*=0.003$) not statistically significant decline in prescriptions of beta-blockers 93% ($p=0.010$) was observed. Furthermore, a significant decrease ($p=0.002$) of clopidogrel prescriptions [42 patients (43%)] and a non-significant decline ($p=0.012$) in the use of acetylsalicylic acid [76

Table 2 Prescriptions of medications with therapeutic guideline recommendations

	Acute coronary syndromes					Stroke				
	Hospital discharge (n=104) %	Week 2 (n=104) %	Week 12 (n=98) %	Week 24 (n=98) %	p-value[a]	Hospital discharge (n=30) %	Week 2 (n=30) %	Week 12 (n=30) %	Week 24 (n=29) %	p-value[a]
Vasodilators	15.4	21.2	19.4	18.3	0.188	0	0	0	0	–
Beta-blockers	96.2	91.3	90.8	92.9	0.010	50.0	46.7	50.0	48.3	0.875
Calcium channel blockers	9.6	8.7	11.2	11.2	0.629	10.0	6.7	13.3	13.8	0.194
ACE inhibitors[b]	64.4	65.4	60.2	60.2	0.380	43.3	40.0	43.3	44.8	0.572
Angiotensin II antagonists	16.3	15.4	19.4	18.4	0.172	13.3	13.3	13.3	13.3	1.000
Lipid-lowering agents	79.8	83.7	82.6	83.7	0.442	66.7	60.0	66.7	65.5	0.682
Clopidogrel	55.8	54.8	52.0	42.9	0.002	26.7	23.3	16.7	20.7	0.479
Ticlopidine	0	1,0	1,0	1,0	0.392	0	0	0	0	
Acetylsalicylic acid	85.6	85.6	78.6	77.6	0.012	56.7	50.0	60.0	65.5	0.525

Adjusted α-level: $\alpha^*=0.05/16=0.003$

[a] Cochran's Q test; [b] (ACE) angiotensin-converting enzyme inhibitors

patients (78%)] occurred in week 24. Of all ACS patients, 11% did not receive any antiplatelet agent at hospital discharge as well as 12% at week 2 and week 12 and 16% at week 24. However, 52% of the patients at HD and 2 weeks later were treated with acetylsalicylic acid and clopidogrel in combination. Furthermore, a decrease in the use of the combination therapy was observed in week 12 (43%) and week 24 (37%), respectively.

Of all patients with stroke, 15 (50%) received a beta-blocker, 13 (43%) used an ACE inhibitor, 3 (10%) used a calcium channel blocker, 20 (67%) used a lipid-lowering agent, 17 (5%) used acetylsalicyclic acid, and 8 (27%) used clopidogrel at the time of hospital discharge (Table 2). No significant changes in medication were observed within 24 weeks. With regard to antiplatelet agent therapy, about 6 out of 30 patients did not receive any treatment throughout the observation time.

Data quality was assessed by comparing the prescribed medication as indicated on the physician questionnaires (n=28) with the medication documented in the health diaries (weeks 1–21). The data showed an agreement of 90.5% between the reports submitted by the patients and the physicians.

Discussion

The present study revealed a remarkably high number of ACS patients receiving antiplatelet medication (89%), beta-blockers (96%), lipid-lowering agents (80%), and ACE inhibitors (64%) when compared with earlier publications. Only the results from the Acute Myocardial Infarction (MITRA 1 + 2) and Myocardial Infarction (MIR) Registries showed a higher treatment rate of patients with ACE inhibitors (76%) at the time of HD (Gottwik et al. 2001). In contrast, EUROASPIRE-II reported that 84% of ACS patients received antiplatelet medication, 66% received beta-blockers, 63% received lipid-lowering agents, and 43% received ACE inhibitors (EUROASPIRE I and II Group 2001). Less positive, however, are the results of the DETECT-Study, reflecting the medication of patients with coronary artery disease in a German outpatient setting (Bischoff et al. 2006). Observed prescription rates for antiplatelet medication were 53%, for beta blockers 57%, for statins 43%, and for ACE inhibitors 50%. Furthermore, on closer examination, the apparently positive results of the present study concerning the antiplatelet medication of ACS patients are also less satisfactory. Only 52% of all ACS patients were treated with acetylsalicylic acid and clopidogrel in combination. These are insufficient results, since the combination of both antiplatelet agents was shown to be highly effective in secondary prevention of vascular events and in preventing coronary stent thrombosis. Compared to acetylsalicylic acid alone, a combination of clopidogrel and acetylsalicylic acid decreases the number of cardiovascular events in patients with ACS by 20% (CURE Study Investigators 2001). In addition, a decline of the combination therapy was observed in week 12 (43%) and week 24 (37%), respectively. Therefore, for at least 9 months the guideline-recommended secondary medical prevention of ACS with the combination of acetylsalicylic acid and clopidogrel was not yet consistently implemented (Hamm et al 2004a, 2004b; Silber et al. 2005). Aside from some medical reasons (e.g., side effects), the cost-containment restrictions ("medication budget") for German physicians might explain the observed failure of guideline-oriented medication. Hypertensive, antiplatelet, and lipid-lowering therapies are also known to reduce the risk of recurrence of cerebrovascular disease (Jamieson 2007). Based on these findings, the medications prescribed to patients with stroke seemed to be in concordance with current guideline recommendations. Specifically, >50% of patients received an antihypertensive medication, >80% of patients received an antithrombotic medication, and about 70% of patients were given a lipid-lowering agent. Several study patients had suffered a cerebral event coded as "unspecified stroke" (ICD-10: I64), which might have included cases of hemorrhagic stroke. This could be an explanation for why six patients (20%) did not receive any antithrombotic medication after HD. Except for antiplatelet medication, no changes in prescriptions were observed during the observation period for ACS patients. However, vasodilators used in cardiac diseases were prescribed more often (an increase of 3%), while beta-blockers had a lower prescription rate after 24 weeks (a decrease of 3%). This may indicate that some of the attending physicians focused on symptomatic treatment of the medical condition. Patients with ACS took an average of six medications and patients with stroke took an average of five medications, which is in the upper range reported in the literature (Hach et al. 2005; Harder et al. 2005). It was also found that polypharmacy can be caused by treatment according to evidence-based therapeutic guidelines, which is particularly problematic for elderly and multi-morbid patients (Meinertz and Kähler 2005). However, the administration of various drugs at various times of the day with different instructions can be very demanding and may result in low compliance, especially for geriatric patients (Kidd and Altmann 2000). The employed method involving a health diary yielded sufficiently high data quality, as supported by the overall high agreement with regard to medication documentation by patients and physicians (>90%). However, it was difficult to motivate the physicians conducting further treatment to participate in this study (physician questionnaire: first contact after HD, n=28), and those who participated did not fully document medication-related infor-

mation, e.g., reasons for a change in medications. The findings of this study are therefore limited to a small sample size. This must especially be kept in mind when interpreting the results of the patients with stroke (n=30). These data were obtained at five hospitals within the Cologne area and approximately 86% of the patients were hospitalised in a tertiary care hospital. Therefore, it is not known with certainty to what degree these results can be generalised. In conclusion, the results of our study as well as the results of the DETECT-study (Bischoff et al. 2006) indicate an undersupply of ACS patient with antiplatelet agents, especially in outpatient care. In particular, the combination therapy with acetylsalicylic acid and clopidogrel seemed to not be sufficient in all cases. Future studies, particularly in German outpatient settings, with longitudinal design and representative samples should focus on this problem.

Acknowledgements The authors wish to thank all patients, physicians, and study nurses who participated in the study. We also are indebted to the staff and physicians of the participating hospitals: Klinik III für Innere Medizin der Universität Köln (Prof. Dr. Höpp), Klinik und Poliklinik für Neurologie der Universität Köln (Prof. Dr. Haupt), Dreifaltigkeits-Krankenhaus Wesseling (Dr. Göke), St. Elisabeth-Krankenhaus Köln (Prof. Dr. Pohl), Eduardus-Krankenhaus Köln (Dr. Witthöft), and St. Lukas Klinik Solingen (Dr. Leopold, Dr. Beckers). This study was supported financially by Sanofi-Aventis Germany GmbH.

Conflict of interest The authors disclose any relevant associations that might pose a conflict of interest.

References

Bertrand ME, Simoons ML, Fox KAA et al (2002) Management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 23:1809–1840

Braunwald E, Antman EM, Beasley JW et al (2002) ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction - summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. J Am Coll Cardiol 40:1366–1374

Bundesärztekammer, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften, Kassenärztliche Bundesvereinigung (2006) Nationale Versorgungs-Leitlinie Chronische KHK. Langfassung Version 1.011. Februar 2006. http://www.versorgungsleitlinien.de/themen/khk/pdf/nvl_khk_lang.pdf (05 July 2006)

CURE Study Investigators (2001) Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 345:494–502

Dimdi. Anatomisch-therapeutisch-chemische-Klassifikation mit Tagesdosen. Amtliche Fassung des ATC-Index mit DDD-Angaben für die Bundesrepublik Deutschland im Jahr 2005. http://www.dimdi.de. (04 November 2005)

EUROASPIRE I and II Group; European Action on Secondary Prevention by Intervention to Reduce Events (2001) Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. Lancet 357:995–1001

Gottwik M, Zahn R, Schiele R et al (2001) Differences in treatment and outcome of patients with acute myocardial infarction admitted to hospitals with compared to without departments of cardiology. Eur Heart J 22:1794–1801

Hach I, Maywald U, Meusel D, König UJ, Kirch W (2005) Continuity of long-term medication use after surgical hospital stay. Eur J Clin Pharmacol 61:433–438

Hamm CW, Arntz HR, Bode C et al (2004a) Leitlinie:. Akutes Koronarsyndrom (ACS).Teil 1: Akutes Koronarsyndrom ohne persistierende ST-Hebung. Z Kardiol 93:72–90

Hamm CW, Arntz HR, Bode C et al (2004b) Leitlinie:. Akutes Koronarsyndrom (ACS).Teil 2: Akutes Koronarsyndrom mit ST-Hebung. Z Kardiol 93:324–341

Hamann G, Weimar C, Glahn J, Busse O, Diener H (2003) Adherence to secondary stroke prevention strategies – results from the German stroke data bank. Cerebrovasc Dis 15:282–288

Harder S, Fischer P, Krause-Schäfer M et al (2005) Structure and markers of appropriateness, quality and performance of drug treatment over a 1-year period after hospital discharge in a cohort of elderly patients with cardiovascular diseases from Germany. Eur J Clin Pharmacol 60:797–805

Himmel W, Kochen MM, Hummers-Pradier E (2004) Drug changes at the interface between primary and secondary care. Int J Clin Pharmacol Ther 42:103–109

Jamieson DG (2007) Secondary Prevention of Ischemic Stroke: Evolution from a stepwise to a risk stratification approach to care. Disease Management 10:273–284

Joint Guidelines issued by the German Neurological Society and the German Stroke Society. Published in: Diener HC, Putzki N, Berlit P (2005) Leitlinien für Diagnostik und Therapie in der Neurologie. Stuttgart: Thieme-Verlag; 3. Auflage:192–214

Kidd KE, Altmann DG (2000) Adherence in social context. Control Clin Trials 21:184S–187S

Krumholz HM, Radford MJ, Wang Y, Chen J, Heiat A, Marciniak TA (1998) National use and effectiveness of beta-blockers for the treatment of elderly patients after acute myocardial infarction: National cooperative cardiovascular project. JAMA 280:623–629

Mandelzweig L, Battler A, Boyko V et al (2006) The second Euro Heart Survey on acute coronary syndromes: characteristics, treatment, and outcome of patients with ACS in Europe and the Mediterranean Basin in 2004. Eur Heart J 27:2285–2293

Meinertz T, Kähler J (2005) Polypharmakotherapie ein Problem der Evidence-based Medicine. Arzneimitteltherapie 23:176–180

Phillips P (1999) New pharmaceutical approaches to stroke prevention, treatment. JAMA 281:2075–2076

Silber S, Albertsson P, Francisco F, The European Society of Cardiology Guidelines for Percutaneous Coronary Intervention (2005) Guidelines for Percutaneous Coronary Interventions: The Task Force for Percutaneous Coronary Interventions of the European Society of Cardiology. Eur Heart J 26:804–847

Taxis K, Schneeweiss S (2003) Frequency and predictors of drug therapy interruptions after hospital discharge under physician drug budgets in Germany. Int J Clin Pharmacol Ther 41:77–82

Weltermann B, Martin C, Adl S, Küching G, Korbonits G, Höpp HW (1997) Verordnungspraxis von Betablockern an der Schnittstelle von stationärer zu ambulanter Versorgung. Gesundheitswesen 59:258–261

Wienbergen H, Schiele R, Gitt AK et al (2001) Aktuelle Verordnungspraxis von CSE-Hemmern bei Entlassung aus der Klinik nach akutem Myokardinfarkt. Z Kardiol 90:394–400

Zeymer U et al (2007) Sekundärprävention der koronaren Herzkrankheit in der Arztpraxis. DMW 132:2367–2370